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EXAMINER	
WOLLENBERGER, LOUIS V	
ART UNIT	PAPER NUMBER
1635	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/554,123	NEVALAINEN, MARJA T.	
	Examiner	Art Unit	
	Louis Wollenberger	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 May 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-53* is/are pending in the application.

4a) Of the above claim(s) *4-7,15-20,25,26,30-33,41-46 and 48-52* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3, 8-14, 21-24, 27-29, 34-40, 47, and 53* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 October 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/29/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims

Applicant draws the Examiner's attention to the substitute specification filed 10/21/05, which contains a listing of claims for examination. The Examiner acknowledges that a second claim set was filed with the original application, but was not clearly marked as a preliminary amendment to the claims. Further the amended claims are not identified with the appropriate identifiers as required by 37 CFR 1.121. For purposes of this examination, and in the interest of compact prosecution, these claims will, however, be entered into the application for search and examination. Accordingly, previous rejections and/or objections to the claims not reiterated herein are withdrawn. However, Applicant's are advised that the substitute specification filed therewith is objected to and has not been entered into the application for the reasons given below.

Claims 1-53 are pending.

Election/Restrictions

Applicant's election without traverse of Group I, claims 1-24, 27-47, drawn to a method of inhibiting prostate cancer cell growth, comprising inhibiting STAT5 activity, in the reply filed on 5/29/08 is acknowledged. In that reply, Applicant further elected Jak2, Stat5b, siRNA, and metastatic cancer cells. In the case of the latter, this is taken to mean metastatic prostate cancer cells in claims 23 and 28. Applicant submits claims 1-24 and 27-47 are representative of the election. The Examiner respectfully disagrees, and submits claims 1-3, 8-14, 21-24, 27-29, 34-40, 47, and 53 read on the elected invention.

Claims 4-7, 15-20, 25, 26, 30-33, 41-46, and 48-52 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 5/29/08. With regard to claims 15, 16, 41, and 42, it is clear upon search and examination that the claims are directed to methods that are related to but distinct from those using an siRNA construct that inhibits the expression of a Stat5 polypeptide such as Stat5b. In the instant case, claims 15, 16, 41, and 42 require inhibiting Stat5 using an inhibitor of a Stat5 kinase such as Jak2, which is materially distinct from a method of inhibiting Stat5 using an siRNA construct that inhibits Stat5 expression. For the same reasons, the different methods lack unity of invention, because they do not share the same or corresponding special technical feature.

While claims 15, 16, 41, and 42 are currently withdrawn, the claims remain eligible for rejoinder should a linking claim be found allowable, as explained in the Restriction Requirement. For example, claims 1 and 2 link the inventions of at least claims 3-21.

Claims 1-3, 8-14, 21-24, 27-29, 34-40, 47, and 53 are examined herein.

Specification

The substitute specification filed 10/21/05 has not been entered because it does not conform to 37 CFR 1.125(b) inasmuch as it is not accompanied by a statement that the substitute specification includes no new matter.

Claim Objections

Applicant is advised that should claim 36 be found allowable, claim 38 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing,

despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). Claim 38 is further objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Claim 8 is objected to because the limitation "the agent that inhibits Stat5 activity" lack literal antecedent basis. The limitation "the inhibitor of Stat5 activity" is preferable, as this antecedent is found in claim 3.

Claim 3 is objected to because of a missing "of" between "the inhibitor" and "Stat5" in line 1 of the claim.

Claims 3, 10, 12, 14, 23, 24, 28, 29, 36, 38, and 40 are objected to for reciting non-elected subject matter. See elections above.

Claim Rejections - 35 USC § 112, first paragraph (written description)

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 2, 21, 22, 23, 27, 28, 47, and 53 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably

convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Factors to be considered in determining whether there is sufficient evidence of possession include the level of skill and knowledge in the art, complete or partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient.

The claims are drawn to methods of inhibiting prostate cancer cell growth in vitro or in a male in need thereof comprising administering an inhibitor of Stat5 activity, and to a pharmaceutical composition comprising an inhibitor of Stat5 activity. In certain embodiments the claims require the inhibitor of Stat5 activity result in prostate cancer cell death. Thus, the claims are extremely broad, embracing any chemical or physical means known or yet-to-be-discovered for inhibiting Stat5, including any small or large molecule, organic or inorganic compound, composition, lipid, nucleic acid, protein or polypeptide.

Adequate written description does not exist in the instant application for all these substances. That is, the specification does not adequately allow persons of ordinary skill in the art to recognize that applicant(s) were in possession of the entire genus of Stat5-inhibiting agents needed to practice the full scope of the methods now claimed. In the instant case, the products required for the methods are recited in terms of their function only, there is no art-recognized correlation between the structure and function, and the specification does not provide the support

needed to enable one skilled in the art to predict with a reasonable degree of confidence the structure of the claimed inventions from a recitation of function. As a result, one of skill in the art would not recognize Applicant was in possession of the methods of using all such substances.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed (pg. 1117). A disclosure in a parent application that merely renders the later- claimed invention obvious is not sufficient to meet the written description requirement; the disclosure must describe the claimed invention with all its limitations. *See Lockwood* , 107 F.3d at 1572, 41 USPQ2d at 1966. An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997).

MPEP 2163 states in part that "The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. See *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406.

A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. The disclosure of only one species encompassed within a genus adequately describes a claim directed to that genus only if the disclosure "indicates that the patentee has invented species sufficient to constitute the gen[us]." See *Enzo Biochem*, 323 F.3d at 966, 63 USPQ2d at 1615; *Noelle v. Lederman*, 355 F.3d 1343, 1350, 69 USPQ2d 1508, 1514 (Fed. Cir. 2004) (Fed. Cir. 2004).

In the instant case, applicants have not satisfied either of these criteria. That is, the instant application discloses no structure common to the genus of Stat5-inhibitory agents, nor species representative of the genus.

While the specification adequately describes certain specific siRNA constructs targeted to the Stat5a or b isoforms or both, and a construct for expressing a dominant negative mutant Stat5 protein (AdDNStat5) (pp. 24-38), said to be capable of inhibiting both Stat5a and b, by fully setting forth their structures and functions, and by describing the materials and methods needed to make and use such agents, adequate written description does not exist for the virtually unlimited number of other inhibitors in the claimed genus. Thus, applicants have not shown possession of the claimed methods using all such agents to inhibit Stat5 in prostate cancer cells, much less cause prostate cancer cell death. For example, aside from a dominant negative construct that inhibits both Stat5a and Stat5b, Applicant has not described any other agent capable of producing prostate cancer cell death. While Applicant contemplates the use of an siRNA against Stat5a or b, Applicant has not described any siRNA capable of producing prostate

cancer cell death. Applicant has not described any siRNA capable of inhibiting both Stat5a and b.

MPEP §2163 states, in part: "[A] patentee of a biotechnological invention cannot necessarily claim a genus after only describing a limited number of species because there may be unpredictability in the results obtained from species other than those specifically enumerated. A patentee will not be deemed to have invented species sufficient to constitute the genus by virtue of having disclosed a single species when … the evidence indicates ordinary artisans could not predict the operability in the invention of any species other than the one disclosed. *In re Curtis*, 354 F.3d 1347, 1358, 69 USPQ2d 1274, 1282 (Fed. Cir. 2004)."

In the instant case, based on the fact that the agent may be one that inhibits at the DNA, RNA, or protein levels, given that Stat5 activity derives from at least two different isoforms, and given that Stat5 activity may be inhibited directly or indirectly, there is sufficient reason to believe there would be a fair degree of variability in the genus of small and large molecule agents capable of inhibiting Stat5 activity and causing prostate cancer cell death.

Accordingly, only methods comprising the use of siRNA and the dominant negative mutant protein meet the written description requirement.

Applicant is reminded that the written description requirement is separate and distinct from the enablement requirement. *In re Barker*, 559 F.2d 588, 194 USPQ 470 (CCPA 1977), cert. denied, 434 U.S. 1064 (1978); *Vas-Cath, Inc.* v. *Mahurkar*, 935 F.2d 1555, 1562, 19 USPQ2d 1111, 1115 (Fed. Cir. 1991).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 2, 21, 22, 27, and 53 are rejected under 35 U.S.C. 102(e) as being anticipated by Shaw et al. (WO 03/026641), as evidenced by Leong et al. (2002) *Oncogene* 21:2846-2853.

Shaw et al. disclosed and claimed a method for using a STAT5B inhibitor to treat prostate carcinoma (page 3, 4, 6, 7, and claim 4, page 44). [Note: Shaw et al. use the term "prostrate carcinoma", which is believed to be an obvious typographical error for the intended term "prostate carcinoma."] Because Shaw et al. taught using specific compounds for treating prostate cancer, Shaw et al. implicitly describes "pharmaceutical" compositions comprising said compounds.

> MPEP 2131.01 states that when the claimed composition or machine is disclosed identically by the reference, an additional reference may be relied on to show that the primary reference has an "enabled disclosure." *In re Samour,* 571 F.2d 559, 197 USPQ 1 (CCPA 1978) and *In re Donohue,* 766 F.2d 531, 226 USPQ 619 (Fed. Cir. 1985).

Methods for making and using STAT5B inhibitors were known in the art, as evidenced by Leong et al. (2002) *Oncogene* 21:2846-2853, who taught antisense oligonucleotides for inhibiting Stat5b in cancer cells.

With regard to claim 22, prostate cancer cell death is considered to be an outcome inherent to inhibiting Stat5b activity. As Shaw et al. disclosed each step and material limitation

claim 22 but is silent with regard to the fate of the prostate cell, and since the Office is not equipped with the resources necessary to test the method of Shaw et al. for such effects, burden is shifted to Applicant to show the method of Shaw et al. would not produce such an effect. MPEP 2112.

Accordingly, Shaw et al. anticipates instant claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 3, 8-14, 23, 24, 28, 29, 34-40, and 47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shaw et al. (WO 03/026641), as applied to claims 1, 2, 21, 22, 27, and 53 above, and further in view of Leong et al. (2002) *Oncogene* 21:2846-2853; Turkson et al. (2000) *Oncogene* 19:6613-6626; Ahonen et al. (2002) *Endocrinology* 143:228-238; and Tuschl et al. (US 20040259247 A1).

Shaw et al. is relied on for the reasons given above.

Shaw et al. does not teach siRNA or specifically inhibiting metastatic prostate cancer cells.

Nevertheless, it would have been obvious to one of skill in the art at the time, and one of skill would have reasonably predicted at the time, that the method of Shaw et al. could be used to inhibit Stat5b in any prostate cancer cell, including those that had metastasized.

Furthermore, in addition to Shaw et al., the prior art taught a strong link between Stat5b expression and many types of cancer, including lymphoma, leukemia, head and neck cancer, and prostate cancer.

For example, Leong et al. taught that targeting Stat5b using antisense oligonucleotides inhibits squamous cell carcinoma of the head and neck (pp. 2846-2853). Leong et al. further state that numerous reports have suggested an association between activation of STAT proteins, including Stat5, and uncontrolled proliferation (page 2846).

Turkson et al. taught that STAT family members, particularly Stat3 and Stat5, are associated with a wide variety of human malignancies, including breast, head and neck, and prostate cancers (pp. 6613-6626, Table 1).

Ahonen et al. taught that "Therapy-based killing of prostate cancer cells may require combined blockade of distinct signaling pathways of several growth factors and cytokines, among which Stat5 proteins may provide a good candidate target."

Shaw et al. specifically recommend and teach using an inhibitor of Stat5b to treat prostate carcinoma.

Accordingly, the prior art is replete with disclosure suggesting a link between Stat5b and cancer, including prostate cancer. As a result, it would have been the normal desire of one of skill in the art at the time of invention to make and use Stat5b inhibitors to inhibit Stat5b expression in any cancer cell, including prostate cancer cells, in vitro or in vivo, to further investigate the role of Stat5b in cancer cell growth in vitro and in vivo, with an eye towards developing methods for treating cancer by, for example, inhibiting Stat5b.

In view of Shaw et al. and Leong et al., it would further have been obvious to use any inhibitor, such as any nucleic acid inhibitor, known to be capable of specifically targeting the Stat5b isoform to treat prostate cancer.

The level of skill and knowledge in the art of RNA interference in mammalian cells at the time of invention was such that the design, preparation, and use of short interfering RNAs (siRNA) against a known gene was conventional, as evidenced by Tuschl et al., who provide a complete blueprint for the design, synthesis, and application of short interfering RNAs for sequence-specific inhibition of gene expression in a mammalian cell in vitro and in vivo.

In view of the wealth of guidance and direction suggesting and teaching that Stat5 proteins such as Stat5b cause or promote cancer cell growth, or, at the least, represent potential therapeutic targets, given that in at least one case in the prior art showed that inhibition of Stat5b inhibits cancer cell growth (Leong et al.), and given that the prior expressly taught and suggested inhibiting Stat5b to treat prostate carcinoma (Shaw et al. and Ahonen et al., respectively), one of skill would reasonably have expected that siRNA-mediated inhibition of Stat5b in prostate cancer cells would inhibit the growth of one or more cells in vivo, and thereby produce an effect representative of treatment of said cancer.

Accordingly, in the absent of convincing evidence to the contrary, the instantly claimed invention would have been *prima facie* obvious to one of skill in the art at the time the invention was made.

Prior art made of record but not currently relied on

The following post-filing art is made of record and is not relied upon, but is considered pertinent to applicant's disclosure.

Xi et al. (2003) Cancer Res. 63:6763-6771 taught that constitutive activation of Stat5b leads to carcinogenesis in vivo.

Kazansky et al. (2003) Cancer Res. 63:8757-8762 taught that inhibiting Stat5b with a dominant negative isoform of Stat5b inhbits the growth, invasive potential, and clonogenic ability of prostate cancer cells, and firmly establish that activation of Stat5b faciliates the progression of prostate cancer.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Louis Wollenberger whose telephone number is (571)272-8144. The examiner can normally be reached on M-F, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James (Doug) Schultz can be reached on (571)272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Louis Wollenberger/
Examiner, Art Unit 1635
August 26, 2008